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Women's values and preferences and health state valuations for thromboprophylaxis during pregnancy: A cross-sectional interview study

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ABSTRACT

Background: Pregnant women with prior venous thromboembolism (VTE) are at risk of recurrence. Prophylaxis with low molecular weight heparin (LWMH) reduces that risk but is inconvenient, costly, and may be associated with increased risks of obstetrical bleeding. The views of pregnant women, crucial when making prophylaxis recommendations, are currently unknown.
Methods: Cross-sectional international multicenter study. We included women with a history of VTE who were either pregnant or planning pregnancy. We provided information regarding risk of VTE recurrence with and without LMWH and determined participant's willingness to receive LMWH prophylaxis through direct choice exercises, preference-elicitation (utilities) for health states (e.g. burden of LMWH prophylaxis), and a probability trade-off exercise.
Results: Of 123 women, more women at high risk than those at low risk of recurrence (86.4% vs. 60.0%; $p = 0.003$) chose to use LMWH. The median threshold reduction in VTE at which women were willing to accept use of LMWH, given a 16% risk of VTE without prophylaxis, was 3% (interquartile range: 1 to 6). Participants' evaluation of the relevant health states varied widely and was unrelated to their direct choices to use or not use LMWH.
Conclusions: Although the majority of women with a previous VTE, pregnant or planning pregnancy choose to take LMWH during pregnancy, a minority –and in low risk women, a large minority– do not. Our results highlight the need for individualized shared decision-making (SDM) in the clinical encounter, and for guideline panels to make weak recommendations in favor of LMWH that make clear the need for SDM.

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1. Introduction

Pregnancy-associated venous thromboembolism (VTE), which may manifest as pulmonary embolism (PE) or deep vein thrombosis (DVT), is an important cause of maternal morbidity and mortality [1,2]. Women with prior VTE are at increased risk of thrombosis during subsequent pregnancies, although the absolute magnitude of that risk remains controversial [1,3–5]. Two randomized trials compared heparin prophylaxis to placebo or no prophylaxis in pregnant women with prior VTE but suffered from major limitations, including very small sample sizes [6,7]. Best estimates of the impact of prophylaxis to prevent recurrent pregnancy-related VTE, therefore, are based primarily on risk estimates from observational studies and indirect evidence from other settings suggesting that low molecular weight heparin (LMWH) decreases the risk of VTE by approximately 70% [1,8].

LMWH, which is recommended in this setting, does not cross the placenta, increase the risk of serious adverse fetal outcomes or significantly increase the risk of thrombocytopenia (<0.1%) or osteoporosis (<1%) [1]. It is, however, expensive, inconvenient, uncomfortable to administer, may be associated with an increased risk of major obstetrical bleeding [1,9], and generally necessitates a planned delivery to permit epidural analgesia [1]. Additionally, women may perceive that LMWH creates an undesirable medicalization of their pregnancy.

Given the competing drawbacks and benefits of prophylaxis, as well as the limitations of the available evidence, the decision to use or not use LMWH is likely to be preference sensitive. In addition to holding different attitudes toward the risk of recurrent thrombosis and the burdens associated with the use of prophylaxis, women are also likely to place varying importance on seeing pregnancy as a normal part of a healthy woman's life, rather than as a medical condition. Although investigators have evaluated patients' values and preferences with respect to anticoagulant therapy in atrial fibrillation [10,11], and to a lesser extent in VTE [12]; a recent systematic review of patient preferences for antithrombotic treatment did not identify any studies addressing pregnant women [13]. We, therefore, addressed this gap in knowledge by determining the values and preferences, and the choices, of women with prior VTE who were currently pregnant or might in the future become pregnant.

2. Materials and methods

We summarize here the methods of our multi-center international cross-sectional interview study. Readers will find further details in a previously published protocol [14].

2.1. Study population and eligibility criteria

We included pregnant women with a history of lower extremity DVT or PE who were considering thromboprophylaxis to prevent recurrent antepartum VTE; women with a history of lower extremity DVT or PE who were planning pregnancy; and women 18 to 45 years of age with a history of lower extremity DVT or PE who might in the future become pregnant. We excluded women who were currently receiving thromboprophylaxis or full-dose anticoagulation, had undergone surgical sterilization (tubal ligation or hysterectomy), had a partner who had undergone a vasectomy, and those unwilling or unable to provide informed consent. The study was approved by the Ethics Committees at all participating institutions and all patients provided written informed consent.

2.2. Recruitment strategy

We prospectively identified women who were currently pregnant or planning a pregnancy as they were referred for counseling and identified women with a history of VTE with the potential to become pregnant by reviewing patient files. We approached women referred for consideration of thromboprophylaxis prior to their consultation and made initial contact with women who were not currently pregnant or planning a pregnancy by letter and then by telephone.

2.3. Study maneuvers

We used standardized scripts developed by the research team. Expert and non-expert clinicians and allied health professionals reviewed and revised the scripts to ensure clinical verisimilitude, as well as understandability and readability by a lay person with a grade 9 reading level. Scripts were translated, where necessary, using professional translators.

2.4. The participant interview

We collected information about the participants' age, highest educational level achieved and current pregnancy status; as well as details regarding their thromboembolic events (including occurrence of PE or DVT, number of events, date of the last event, presence or absence of precipitating factors prior to their event, known hypercoagulable states, family history of VTE, type and duration of treatment for their event(s), completeness of their recovery [presence or absence of residual chest pain or shortness of breath, and/or residual leg swelling, pain or discoloration]), and presence or absence of prior experience with injection of prophylactic doses of LMWH during pregnancy. Patients were classified as being at low or high risk for recurrent VTE during pregnancy based on precipitating factors associated with their initial event. Women were considered lower risk for antepartum recurrence if their previous event was associated with a major transient risk factor (leg casting, major surgery [spinal or general anesthetic for at least 30 min], significant medical illness with hospitalization for at least three days, immobilization for at least three days, active malignancy) and they had no known thrombophilia. Women were considered higher risk if their event had been unprovoked, estrogen-related, or they were known to have a thrombophilia.

2.5. Direct choice exercises

We determined participants' willingness to receive LMWH prophylaxis through direct choice exercises using decision boards. Women initially completed what we refer to as the real-life scenario (representing the best estimate of their personal risk of recurrence), followed in order by hypothetical scenarios, the visual analog scale, the probability trade-off exercise, a review of their answers, and finally questions to examine their understanding of the scenarios.

2.5.1. Real-life scenario

We initially presented women with a decision board that included the probabilities of developing VTE during pregnancy given the characteristics of their prior event. We constructed two boards, one for lower and one for higher risk of recurrence. Women at low risk were presented with a potential baseline risk of antepartum recurrence of 0 to 5% and high risk women with a baseline antepartum risk of 5 to 10%. To ensure optimal understanding, the risk of recurrence with and without LMWH prophylaxis was presented in three different ways: table, bar chart and pictograph (Fig. 1).

For the VTE health state, we instructed women to consider their previous venous thromboembolic event. We instructed women with previous experience in the use of prophylactic LMWH for 2 weeks or longer during pregnancy to consider their previous experience when making a decision. We prepared a description of the experience of LMWH use throughout pregnancy for women without prior experience with LMWH prophylaxis during pregnancy (Appendix 1).

After they reviewed this information, participants decided whether or not they were willing to use LMWH during their current or future pregnancy. Following the interview, women referred for consideration of prophylaxis met with their health care provider and, if desired,